

WHAT IS CLAIMED IS:

1. A molecular detector for detecting single-molecules in solution comprising:

a solution reservoir;

at least one biofunctionalized nanometer-scale mechanical resonator disposed within the reservoir;

a detector in signal communication with the at least one resonator for measuring the mechanical displacement of the resonator.

2. A molecular detector as described in claim 1, wherein the at least one resonator comprises a resonator selected from the group consisting of: vibrational resonators, rotational resonators, torsional resonators and composite resonators.

3. A molecular detector as described in claim 1, wherein the at least one resonator is a notched vibrational cantilever.

4. A molecular detector as described in claim 1, wherein the at least one resonator is biofunctionalized with a receptor.

5. A molecular detector as described in claim 4, further comprising a substrate disposed within the reservoir and adjacent to the at least one resonator, wherein the substrate is biofunctionalized with a ligand capable of molecular interaction with the receptor.

6. A molecular detector as described in claim 4, further comprising a substrate disposed within the reservoir and adjacent to the at least one resonator, wherein the substrate is biofunctionalized with a receptor capable of molecular interaction with a ligand wherein the ligand is capable of molecular interaction with the receptor on the resonator.

7. A molecular detector as described in claim 1, comprising at least two resonators arranged adjacent to one another, wherein at least one of the resonators is biofunctionalized with a receptor to form a receptor resonator and at least one of

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the resonators adjacent to the receptor resonator is biofunctionalized with a ligand capable of molecular interaction with the receptor.

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8. A molecular detector as described in claim 1, comprising at least two resonators arranged adjacent to one another,

wherein at least one of the resonators is a driver resonator comprising a driving element capable of mechanically displacing the driver resonator at a chosen frequency, wherein the driver resonator is biofunctionalized with a receptor;

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and at least one of the resonators adjacent to the driver resonator is biofunctionalized with a ligand capable of molecular interaction with the receptor on the driver resonator.

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9. A molecular detector as described in claim 1, comprising at least three resonators arranged adjacent to one another,

wherein at least one of the resonators is a driver resonator comprising a driving element capable of mechanically displacing the first driver resonator at a chosen frequency;

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wherein at least one of the resonators is a second driver resonator comprising a driving element capable of mechanically displacing the second driver resonator at a chosen frequency;

and at least one of the resonators is a follower resonator disposed between the two driver resonators and biofunctionalized with a ligand;

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wherein the driver resonators are driven in antiphase, and wherein at least one of the driver resonators is biofunctionalized with a receptor capable of molecular interaction with the ligand on the follower resonator.

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10. A molecular detector as described in claim 8 or 9 wherein the driver is a piezoelectric device.

11. A molecular detector as described in claim 1, wherein the at least one resonator is made from a material selected from the group consisting of: silicon oxide, silicon, silicon carbide and gallium arsenide.

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12. A molecular detector as described in claim 1, wherein the detector is integral with the resonator.

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13. A molecular detector as described in claim 1, wherein the detector is a piezoresistive transducer.

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14. A molecular detector as described in claim 13, wherein the transducer is made of p+ doped silicon.

15. A molecular detector as described in claim 1, wherein the detector is an optical detector.

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16. A molecular detector as described in claim 1, wherein the detector is a lock-in detector.

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17. A molecular detector as described in claim 1, wherein the resonator has a thickness between about 10nm and  $1\mu\text{m}$ , a width between about 10nm and  $1\mu\text{m}$ , and a length between about  $1\mu\text{m}$  and  $10\mu\text{m}$ .

18. A molecular detector as described in claim 1, wherein the resonator has a resonance motion vacuum frequency between about 0.1 and 12MHz.

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19. A molecular detector as described in claim 1, wherein the resonator has a force constant between about 0.1mN/m and 1 N/m.

20. A molecular detector as described in claim 1, wherein the resonator has a Reynolds number between about 0.001 and 2.0.

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21. A molecular detector as described in claim 1, wherein the resonator has a mass loading coefficient between about 0.3 and 11.

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22. A molecular detector as described in claim 1, having a force sensitivity of about  $8\text{fN}/\sqrt{\text{Hz}}$  or greater.

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23. A molecular detector as described in claim 1, biofunctionalized to detect a receptor/ligand interaction.

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24. A molecular detector as described in claim 1, biofunctionalized to detect DNA hybridization.

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25. A molecular detector as described in claim 1, biofunctionalized to detect a chemical bond.

26. A molecular detector as described in claim 1, biofunctionalized to detect protein unfolding.

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*Similar to d. 7*  
27. A molecular detector system comprising:  
at least one microfluidic channel;  
at least one array of molecular detector devices disposed within the at least one microfluidic channel, wherein the at least one array comprises a plurality of biofunctionalized nanometer-scale mechanical resonators each resonator having at least one detector in signal communication therewith for measuring the resonance motion of the resonator.

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*Similar to d. 9*  
28. A molecular detector system as described in claim 27, wherein the plurality of resonators has at least two different biofunctionalizations.

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29. A method for forming a molecular detector comprising:  
supplying a substrate;  
depositing a photoresist on the substrate;  
exposing a pattern comprising the resonator on the photoresist;  
etching the substrate to form the resonator; and  
removing the photoresist.

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30. The method according to claim 29 wherein the pattern is formed by direct write e-beam lithography.

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31. A method of detecting a molecule of interest comprising the steps of:  
providing a molecular detector comprising a biofunctionalized nano-scale  
resonator adapted to move in response to the thermal motion of a solution, the  
molecular detector further comprising a detector disposed thereon, the detector  
being designed to monitor the mechanical displacement of the resonator;

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placing the molecular detector into a solution such that the resonator is  
mechanically displaced based on the thermal motion of the solution and such that  
in the presence of a species capable of molecular interaction with the  
biofunctionalized resonator, the mechanical displacement of the resonator is  
altered; and

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measuring the mechanical displacement of the resonator such that a change  
in the mechanical displacement of the resonator is communicated to a user.

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32. A method of detecting a molecule of interest comprising utilizing a  
molecular detector according to claim 1.

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